Sequence Listing

<110> Henry B. Lowman, Leonard G. Presta, Paula M. Jardieu, John Lowe

<120> Anti-IgE Antibodies and Method of Improving Polypeptides

<130> P1123R1

<140> US 09/109,207
<141> 1998-06-30

<150> US 60/051,554
<151> 1997-07-03

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aaaagttaat cttttcaaca gctgtcataa agttgtcacg gccgagactt 350

atagtcgctt tgtttttatt ttttaatgta tttgtaacta gaattcgagc 400

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atcgcatttc ttcttgcatc tatgttcgtt ttttctattg ctacaaacgc 500

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1

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3

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        cgtgcaccca actgatcttc agcatctttt actttcacca gcgtttctgg 5850

        gtgagcaaaa acaggaaggc aaaatgccgc aaaaaaggga ataagggcga 5900
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        cacggaaatg ttgaatactc atactcttcc tttttcaata ttattgaagc 5950

        atttatcagg gttattgtct catgagcgga tacatatttg aatgtattta 6000

 20     gaaaaataaa caaatagggg ttccgcgcac atttccccga aaagtgccac 6050

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        <213> Mus musculus
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                         20                 25                  30

        Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Phe Pro Gly Asn Lys
                         35                 40                  45
 40
        Leu Glu Trp Met Gly Ser Ile Thr Tyr Asp Gly Ser Ser Asn Tyr
                         50                 55                  60

        Asn Pro Ser Leu Lys Asn Arg Ile Ser Val Thr Arg Asp Thr Ser
 45                      65                 70                  75

        Gln Asn Gln Phe Phe Leu Lys Leu Asn Ser Ala Thr Ala Glu Asp
                         80                 85                  90

 50     Thr Ala Thr Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                         95                 100                 105

        Trp His Phe Ala Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser
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 55
        Ser


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                20                  25                      30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
                35                  40                      45

Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
                50                  55                      60

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser
                65                  70                      75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                80                  85                      90

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                95                  100                     105

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                110                 115                     120

Ser
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<211> 121
<212> PRT
<213> Homo sapiens

<220>
<221> unsure
<222> 30, 104-108
<223> unknown amino acid

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Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Xaa
                20                  25                      30

Ser Asp Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
                35                  40                      45

Leu Glu Trp Val Ala Val Ile Ser Asn Gly Ser Asp Thr Tyr Tyr
                50                  55                      60

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser
                65                  70                      75

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                80                  85                      90
```

6

```
           Thr Ala Val Tyr Tyr Cys Ala Arg Asp Ser Arg Phe Phe Xaa Xaa
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       Ser

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       <212> PRT
       <213> Mus musculus
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       <400> 5
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          1               5               10                  15

 20    Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp
                        20              25                  30

       Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
                        35              40                  45
 25
       Gln Pro Pro Ile Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Gly Ser
                        50              55                  60

       Glu Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
 30                     65              70                  75

       Thr Leu Asn Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Phe
                        80              85                  90

 35    Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Ala Gly
                        95              100                 105

       Thr Lys Leu Glu Ile Lys
                        110
 40
       <210> 6
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       <212> PRT
       <213> Artificial
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       <221> Artificial
       <222> 1-111
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          1               5               10                  15

 55    Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
                        20              25                  30

       Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
                        35              40                  45
 60
       Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
                        50              55                  60
```

7

```
         Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                     65              70                  75

  5      Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
                     80              85                  90

         Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
                     95             100                 105
 10
         Thr Lys Val Glu Ile Lys
                     110


         <210> 7
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         <212> PRT
         <213> Homo sapiens


         <220>
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         <222> 33-34
         <223> unknown amino acid


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          1               5                  10                  15

         Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
                     20              25                  30
 30
         Ile Ser Xaa Xaa Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                     35              40                  45

         Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Glu Ser
 35                  50              55                  60

         Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                     65              70                  75

 40      Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
                     80              85                  90

         Tyr Cys Gln Gln Tyr Asn Ser Leu Pro Tyr Thr Phe Gly Gln Gly
                     95             100                 105
 45
         Thr Lys Val Glu Ile Lys
                     110


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         <212> PRT
         <213> Artificial


         <220>
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         <222> 1-114
         <223> Light chain sequence derived from MAE11


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          1               5                  10                  15
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8

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        Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val Asp
                     20                  25                  30

        Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
5                        35                  40                  45

        Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
                     50                  55                  60

10      Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                     65                  70                  75

        Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
                     80                  85                  90
15
        Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
                     95                  100                 105

        Thr Lys Val Glu Ile Lys Arg Thr Val
20                       110


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    <211> 114
    <212> PRT
25  <213> Artificial

    <220>
    <221> Artificial
    <222> 1-114
30  <223> Light chain sequence derived from MAE11

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         1               5                  10                  15
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        Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
                     20                  25                  30

        Tyr Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
·40                      35                  40                  45

        Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
                     50                  55                  60

45      Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                     65                  70                  75

        Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
                     80                  85                  90
50
        Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
                     95                  100                 105

        Thr Lys Val Glu Ile Lys Arg Thr Val
55                       110

    <210> 10
    <211> 114
    <212> PRT
60  <213> Artificial

    <220>
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9

<400> 10
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Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
  1               5                  10                      15

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
                20                  25                      30

Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
                35                  40                      45

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
                50                  55                      60

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                65                  70                      75

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
                80                  85                      90

Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
                95                  100                     105

Thr Lys Val Glu Ile Lys Arg Thr Val
                110
```

<400> 11
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
  1               5                  10                      15

Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
                20                  25                      30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
                35                  40                      45

Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr
                50                  55                      60

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
                65                  70                      75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                80                  85                      90

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                95                  100                     105

Trp His Phe Ala Val Trp Gly Gln Gly
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10

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<211> 114
<212> PRT
<213> Artificial

<220>
<221> Artificial
<222> 1-114
<223> Heavy chain sequence derived from MAE11

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Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
                20                  25                  30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
                35                  40                  45

Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
                50                  55                  60

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
                65                  70                  75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                80                  85                  90

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                95                  100                 105

Trp His Phe Ala Val Trp Gly Gln Gly
                110


<210> 13
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<212> PRT
<213> Artificial

<220>
<221> Artificial
<222> 1-218
<223> Light chain sequence derived from MAE11

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Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Asp
                20                  25                  30

Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly
                35                  40                  45

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
                50                  55                  60

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                65                  70                  75
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```
         Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
                      80                  85                  90

 5       Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
                      95                 100                 105

         Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
                     110                 115                 120
10
         Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
                     125                 130                 135

         Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
15                   140                 145                 150

         Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
                     155                 160                 165

20       Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                     170                 175                 180

         Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
                     185                 190                 195
25
         Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
                     200                 205                 210

         Lys Ser Phe Asn Arg Gly Glu Cys
30                   215

         <210> 14
         <211> 451
         <212> PRT
35       <213> Artificial

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           1           5                  10                  15
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         Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
                      20                  25                  30

         Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
50                    35                  40                  45

         Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
                      50                  55                  60

55       Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
                      65                  70                  75

         Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                      80                  85                  90
60
         Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                      95                 100                 105
```

12

```
          Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                          110                 115                 120

  5       Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
                          125                 130                 135

          Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                          140                 145                 150
 10
          Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
                          155                 160                 165

          Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
 15                       170                 175                 180

          Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
                          185                 190                 195

 20       Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
                          200                 205                 210

          Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
                          215                 220                 225
 25
          Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
                          230                 235                 240

          Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
 30                       245                 250                 255

          Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
                          260                 265                 270

 35       Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
                          275                 280                 285

          Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
                          290                 295                 300
 40
          Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
                          305                 310                 315

          Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
 45                       320                 325                 330

          Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
                          335                 340                 345

 50       Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
                          350                 355                 360

          Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
                          365                 370                 375
 55
          Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                          380                 385                 390

          Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
 60                       395                 400                 405

          Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
```

13

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
                425   430   435

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
                440   445   450

Lys

<210> 15
<211> 218
<212> PRT
<213> Artificial

<220>
<221> Artificial
<222> 1-218
<223> Light chain sequence derived from MAE11

<400> 15
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
  1   5   10   15

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val Asp
                20   25   30

Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                35   40   45

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
                50   55   60

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                65   70   75

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
                80   85   90

Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
                95   100   105

Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
                110   115   120

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
                125   130   135

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
                140   145   150

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
                155   160   165

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                170   175   180

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
                185   190   195

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr

14

Lys Ser Phe Asn Arg Gly Glu Cys
                        215

<210> 16
<211> 451
<212> PRT
<213> Artificial

<220>
<221> Artificial
<222> 1-451
<223> Heavy chain sequence derived from MAE11

<400> 16
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
  1   5   10   15

Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
                20   25   30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
                35   40   45

Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
                50   55   60

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
                65   70   75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                80   85   90

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                95   100   105

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                110   115   120

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
                125   130   135

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                140   145   150

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
                155   160   165

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                170   175   180

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
                185   190   195

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
                200   205   210

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
                215   220   225

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly

       Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                       245   250   255
 5
       Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
                       260   265   270

       Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
 10   275   280   285

       Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
                       290   295   300

 15   Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
                       305   310   315

       Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                       320   325   330
 20
       Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
                       335   340   345

       Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
 25   350   355   360

       Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
                       365   370   375

 30   Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                       380   385   390

       Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
                       395   400   405
 35
       Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                       410   415   420

       Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 40   425   430   435

       Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
                       440   445   450

 45   Lys

       <210> 17
       <211> 218
 50   <212> PRT
       <213> Artificial

       <220>
       <221> Artificial
 55   <222> 1-218
       <223> Light chain sequence derived from MAE11

       <400> 17
       Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
 60   1   5   10   15

       Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val Asp

Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
              35   40   45

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
              50   55   60

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
              65   70   75

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
              80   85   90

Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
              95   100   105

Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
             110   115   120

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
             125   130   135

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
             140   145   150

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
             155   160   165

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
             170   175   180

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
             185   190   195

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
             200   205   210

Lys Ser Phe Asn Arg Gly Glu Cys
             215

<210> 18
<211> 451
<212> PRT
<213> Artificial

<220>
<221> Artificial
<222> 1-451
<223> Heavy chain sequence derived from MAE11

<400> 18
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
  1   5   10   15

Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
             20   25   30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
             35   40   45

Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr

       Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
                        65   70   75
  5

       Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                        80   85   90

       Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
  10   95   100   105

       Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                        110   115   120

  15   Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
                        125   130   135

       Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                        140   145   150
  20

       Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
                        155   160   165

  25   Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                        170   175   180

       Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
                        185   190   195

  30   Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
                        200   205   210

       Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
                        215   220   225
  35

       Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
                        230   235   240

  40   Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                        245   250   255

       Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
                        260   265   270

  45   Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
                        275   280   285

       Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
                        290   295   300
  50

       Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
                        305   310   315

  55   Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                        320   325   330

       Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
                        335   340   345

  60   Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
                        350   355   360

```
Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
                365             370             375

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                380             385             390

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
                395             400             405

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                410             415             420

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
                425             430             435

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
                440             445             450

Lys
```

```
<210> 19
<211> 218
<212> PRT
<213> Artificial

<220>
<221> Artificial
<222> 1-218
<223> Light chain F(ab) sequence derived from MAE11

<400> 19
Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
  1               5               10              15

Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val Asp
                20              25                  30

Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                35              40                  45

Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
                50              55                  60

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                65              70                  75

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
                80              85                  90

Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
                95              100             105

Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
                110             115                 120

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
                125             130                 135

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
                140             145                 150
```

19

```
       Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
                   155                 160                 165

       Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
  5                    170                 175                 180

       Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
                       185                 190                 195

 10    Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
                       200                 205                 210

       Lys Ser Phe Asn Arg Gly Glu Cys
                       215
 15
       <210> 20
       <211> 229
       <212> PRT
       <213> Artificial
 20
       <220>
       <221> Artificial
       <222> 1-229
       <223> Heavy chain F(ab) sequence derived from MAE11
 25
       <400> 20
       Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
          1               5                   10                  15

 30    Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
                        20                  25                  30

       Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
                        35                  40                  45
 35
       Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
                        50                  55                  60

       Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
 40                     65                  70                  75

       Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                        80                  85                  90

 45    Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                        95                  100                 105

       Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                        110                 115                 120
 50
       Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
                        125                 130                 135

       Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
 55                     140                 145                 150

       Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
                        155                 160                 165

 60    Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                        170                 175                 180
```

```
        Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
                    185                 190                 195

        Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 5                  200                 205                 210

        Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
                    215                 220                 225

10      Lys Thr His Thr


        <210> 21
        <211> 229
15      <212> PRT
        <213> Artificial

        <220>
        <221> Artificial
20      <222> 1-229
        <223> Heavy chain F(ab) derived from MAE11

        <400> 21
        Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
25        1                 5                 10                  15

        Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
                    20                  25                  30

·30     Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
                    ·35                 40                  45·

        Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr
                    50                  55                  60
35
        Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
                    65                  70                  75

        Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
40                  80                  85                  90

        Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                    95                  100                 105

45      Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                    110                 115                 120

        Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
                    125                 130                 135
50
        Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                    140                 145                 150

        Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
55                  155                 160                 165

        Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                    170                 175                 180

60      Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
                    185                 190                 195
```

```
        Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
                        200                 205                 210

        Ser Asn Thr Lys Val Asp Lys.Lys Val Glu Pro Lys Ser Cys Asp
  5                     215                 220                 225

        Lys Thr His Thr


 10     <210> 22
        <211> 248
        <212> PRT
        <213> Artificial

 15     <220>
        <221> Artificial
        <222> 1-248
        <223> sFv sequence derived from MAE11

 20     <400> 22
        Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
          1               5                  10                  15

        Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
 25                     20                  25                  30

        Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
                        35                  40                  45

 30     Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
                        50                  55                  60

        Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
                        65                  70                  75
 35
        Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                        80                  85                  90

        Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
 40                     95                  100                 105

        Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                        110                 115                 120

 45     Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly
                        125                 130                 135

        Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
                        140                 145                 150
 50
        Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val
                        155                 160                 165

        Asp Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
 55                     170                 175                 180

        Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu
                        185                 190                 195

 60     Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                        200                 205                 210
```

```
   Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
                   215                 220                 225

   Tyr Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln
                   230                 235                 240

   Gly Thr Lys Val Glu Ile Lys Arg
                   245


<210> 23
<211> 248
<212> PRT
<213> Artificial

<220>
<221> Artificial
<222> 1-248
<223> sFv sequence derived from MAE11

<400> 23
   Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
     1               5                  10                  15

   Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
                    20                  25                  30

   Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
                    35                  40                  45

   Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr
                    50                  55                  60

   Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
                    65                  70                  75

   Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                    80                  85                  90

   Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                    95                 100                 105

   Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                   110                 115                 120

   Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly
                   125                 130                 135

   Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
                   140                 145                 150

   Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val
                   155                 160                 165

   Asp Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                   170                 175                 180

   Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu
                   185                 190                 195

   Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                   200                 205                 210
```

```
    Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr
                    215             220             225

    Tyr Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln
                    230             235             240

    Gly Thr Lys Val Glu Ile Lys Arg
                    245


<210> 24
<211> 218
<212> PRT
<213> Artificial

<220>
<221> Artificial
<222> 1-218
<223> Light chain F(ab)'2 sequence derived from MAE11

<400> 24
    Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val
     1               5                   10                  15

    Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val Asp
                    20                  25                  30

    Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                    35                  40                  45

    Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
                    50                  55                  60

    Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                    65                  70                  75

    Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr
                    80                  85                  90

    Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
                    95                  100                 105

    Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
                    110                 115                 120

    Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
                    125                 130                 135

    Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
                    140                 145                 150

    Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
                    155                 160                 165

    Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                    170                 175                 180

    Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
                    185                 190                 195

    Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
                    200                 205                 210
```

24

```
       Lys Ser Phe Asn Arg Gly Glu Cys
                       215


   <210> 25
   <211> 233
   <212> PRT
   <213> Artificial

   <220>
   <221> Artificial sequence
   <222> 1-233
   <223> Heavy chain F(ab)'2 sequence derived from MAE11

   <400> 25
   Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
     1               5                  10                  15

   Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
                    20                  25                  30

   Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
                    35                  40                  45

   Leu Glu Trp Val Ala Ser Ile Thr Tyr Asp Gly Ser Thr Asn Tyr
                    50                  55                  60

   Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
                    65                  70                  75

   Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
                    80                  85                  90

   Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
                    95                  100                 105

   Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                    110                 115                 120

   Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
                    125                 130                 135

   Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                    140                 145                 150

   Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
                    155                 160                 165

   Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                    170                 175                 180

   Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
                    185                 190                 195

   Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
                    200                 205                 210

   Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
                    215                 220                 225

   Lys Thr His Thr Cys Pro Pro Cys
                    230
```

<210> 26
<211> 233
<212> PRT
<213> Artificial

<220>
<221> Artificial
<222> 1-233
<223> Heavy chain F(ab)'2 sequence derived from MAE11

<400> 26

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly
  1               5                  10                  15

Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser Ile Thr
              20                  25                  30

Ser Gly Tyr Ser Trp Asn Trp Ile Arg Gln Ala Pro Gly Lys Gly
              35                  40                  45

Leu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr
              50                  55                  60

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser
              65                  70                  75

Lys Asn Thr Phe Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
              80                  85                  90

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser His Tyr Phe Gly His
              95                  100                 105

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
              110                 115                 120

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
              125                 130                 135

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
              140                 145                 150

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
              155                 160                 165

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
              170                 175                 180

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
              185                 190                 195

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
              200                 205                 210

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
              215                 220                 225

Lys Thr His Thr Cys Pro Pro Cys
              230
```

<210> 27
<211> 45
<212> DNA

<213> Artificial

<220>
<221> Artificial
<222> 1-45
<223> Stop-Template Oligos for First-Round Mutagenesis

<400> 27
acctgccgtg ccagttaata agtctaataa gaaggtgata gctac 45

<210> 28
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       aag 53


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60
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<220>
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<223> unknown base

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